Prevalence of Autoantibodies to Cardiac Troponin T in Healthy Blood Donors

To the Editor:

Recently, human IgG reactive with cardiac troponin (cTn) I has received attention as a potential cause of false-negative results in some immunoassays for that antigen (1) and was further suggested as a possible contributor to idioopathic cardiomyopathy (2, 3) and poor outcome after myocardial infarction (4). The incidence of autoantibodies to cTnI is high in apparently healthy blood donors (12.7%) as well as in sample cohorts characterized on the basis of clinical biomarkers associated with cardiac, infectious, and autoimmune diseases (5). We report that autoantibodies reactive with the cTn T isoform have a similar prevalence to that seen for the I isoform.

Briefly, frozen plasma and serum samples from apparently healthy blood donors (n = 467), all of which had been approved for research use by the institutional review board, were obtained from the Abbott Laboratories specimen bank and thawed at 2–8 °C before use. The average age of the individuals donating these samples was 39.7 years (range 18–72 years), and the sex distribution was 47:53 male to female. A direct chemiluminescent microplate assay was modeled on that previously reported for anti-cTnI (5); with the exception that recombinant cTnT (Biospecific) was used as the capture antigen. A murine antihuman IgG (sub-type IgG2b, κ, Abbott Diagnostics Division), which recognized all human IgG subtypes but had minimal or no reactivity toward human IgM or IgA or rabbit, sheep, or goat IgG, was used as the detection conjugate. Positive samples were confirmed by inhibition with the antigen by use of a method already reported (5). A low-control pool (composed of 24 individual samples within the 25th–50th percentile response range) was used to assess the relative reactivity of each sample. The analyses were carried out on a Berthold Mithras microplate reader (Berthold Technologies, http://www.bertholdtech.com/; software: MikroWin 2000 version 4.34, MikroTek Laborsysteme [http://www.mikrotek.de]). Data were analyzed with MedCalc® version 9.4.3.0 software (http://www.medcalc.be/).

A box-and-whiskers plot illustrating the results is shown in Fig. 1. In the blood donor samples the median response (sample/low control) (95% CI) was 1.300 (1.100–1.400). Statistical outliers above a sample/low control value of 5.3 were categorized as positive responders. In this screening 46 of 467 (9.9%) of samples were positive responders. This positive response rate was not significantly different from that reported for autoantibodies to cTnI (5). In the case of autoantibodies to cTnI, there was an increased incidence of anti-cTnI in males compared to females (15.7 vs 9.9%, P = 0.0361). We found no significant sex-based difference in the positive response rate or the median response for anti-cTnT. Similar to the results for anti-cTnI, the median inhibition of the autoantibodies to the cTnT binding surface by free antigen in solution was 58% (range 28%–95%). The median response of positive responders in the absence of antigen, i.e., on microplates coated only with bovine serum albumin, was only 1.4% of that in the presence of cTnT, similar to that observed with an unrelated antigen (prostate-specific antigen, 1.8%).

Fig. 1. Prevalence of human IgG reactive with cTnT in healthy blood donors.

Box-and-whisker plot: the central box represents the 25th–75th percentile response (points removed for clarity), the middle line represents the median, and the horizontal line extends from the minimum to the maximum value, excluding statistical outliers (open symbol: upper quartile plus 1.5 times the interquartile range; closed symbol: upper quartile plus 3 times the interquartile range) displayed as separate points.

Letters to the Editor
In contrast to our results, Leuschner et al. (4) have reported the absence of autoantibodies to either cTnI or cTnT (titer >1:160) in a healthy population. In their study of cardiomyopathy patients, the anti-cTnI positive rate increased to 7%–9.2%, whereas the anti-cTnT rate remained very low (0.5%–1.7%). We attribute the lower sensitivity in detecting anti-cTnT to the differences between the indirect sandwich assay format used by those authors vs the direct format we used in this report.

To date, the effect of circulating autoantibodies to cTnT, either as an interfering factor in cTnT immunoassays or a pathophysiological indicator, has yet to be elucidated. However, their high prevalence should prompt more investigation.

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References

Distribution and Correlates of Midregional Proadrenomedullin in the General Population

To the Editor:

Adrenomedullin (ADM)1 is a multifunctional peptide hormone expressed in most tissues and in multiple cell types in response to cellular stress, ischemia, and hypoxia. These characteristics indicate that ADM may have a role in protection against cellular injury and therefore is a promising biomarker of disease (1). Increased ADM concentrations have been reported in multiple diseases; however, the results between studies have been inconsistent, perhaps owing to technical difficulties in measuring ADM (2).

We used the previously described immunoluminometric sandwich assay (2) (Brahms) to measure MR-proADM in 5258 fasting individuals from the cardiovascular cohort of the population-based Malmö Diet and Cancer Study who attended a baseline visit between 1991 and 1996 (3). We studied the relation of MR-proADM with 23 other baseline variables (Table 1) ascertained as described previously (3), including plasma markers of inflammation (high-sensitivity C-reactive protein; Tina-quant, Roche Diagnostics), renal function (cystatin C; N Latex Cystatin, Dade Behring), and cardiac wall stress [N-terminal pro-B-type natriuretic peptide (NT-proBNP); Dimension RxL, Dade-Behring]. Plasma markers were measured from fasting plasma samples that had been frozen at −80 °C immediately after collection without previ-

1 Nonstandard abbreviations: ADM, adrenomedullin; MR-proADM, midregional proadrenomedullin; NT-proBNP, N-terminal pro-B-type natriuretic peptide.